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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/700,643	02/02/2001	Hirokazu Matsumoto	2523US0P	5991

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EXAMINER	
NGUYEN, BAO THUY L	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/700,643	MATSUMOTO ET AL.	
	Examiner	Art Unit	
	Bao-Thuy L. Nguyen	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *1-3,12,13,16,17 and 22-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-11,14,15,18-21 and 25-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-31* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election and request for reconsideration filed 12/04/04 has been received. In response to Applicant request for rejoinder of some of the claims, the election/restriction requirement dated 11/10/2003 is withdrawn in favor of the instant action.

2. The examiner would like to thank Applicant's representative, Elaine Ramesh, for the courtesy extended to examiner during a telephone conference on March 11, 2004.

Election/Restrictions

3. Restriction is required under 35 U.S.C. 121 and 372.

4. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

5. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

- Subcombination A:

  The following claim(s) are generic linking claims for Groups I and II: 1, 2, 7-9, 12-14, 16, 17, and 26-30.

  Group I, claim(s) 3, 23, 35 and 31, drawn to monoclonal antibody P2L-1Ca and method using therefor.

  Group II, claim(s) 3, 24, 25 and 31, drawn to monoclonal antibody P2L-2Ca and method using therefor.

- Subcombination B:

  The following claims are generic linking claims for Groups III and IV: 4, 5, 7-9, 10, 11, 14, 15, 18, 19, 20 and 26-30.

Group III, claim(s) 6, 21, 25, 31, drawn to monoclonal antibody P2L-1Ta and method using therefor.

Group IV, claim(s) 22, 25 and 31, drawn to monoclonal antibody P2L-1Ta and method using therefor.

- The following claims are generic combination claims linking subcombinations A and B together:

Claim(s) 8 and 14, drawn to method for detecting 19P2 ligand therefor.

6. Applicant is required, in reply to this action, to elect a single group to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

If applicant elects, for example, a subcombination rather than a combination, upon allowance of the subcombination, the combination will be rejoined.

7. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: Inventions V and I-IV are related as combination and subcombination, respectively. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations. In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the patentability of the combination is not predicated on either subcombination along. The subcombination has utility by itself.

8. During a telephone conversation with Elaine Ramesh on March 11, 2004 a provisional election was made with traverse to prosecute the invention of Group III (monoclonal antibody P2L-1Ta), claims 4-11, 14, 15, 18-21 and 25-31. Affirmation of this election must be made by applicant in replying to this Office action. Claims 1-3, 12-13, 16-17 and 22-24 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

9. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112, second paragraph

10. Claims 4-11, 14, 15, 18-21 and 25-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 5 and 6, "A monoclonal antibody" should be changed to -The monoclonal antibody— for clarity.

Claims 7 and 8 are vague and indefinite because they are methods with no method steps. The claims are also vague because they are dependent on non-elected claim 1. Furthermore, claims 7 and 8 are in improper form because they referenced two set of claims with different features. See MPEP § 608.01(n). Claim 7 and 8 also appear to be duplicate.

Although claim 8 differs from 7 in that it recites the use of "the antibody as claim in claim 1", whereas claim 7 recites the use of "the *monoclonal* antibody as claim in claim 1", these claims are essentially the same since claim 1 recites a "monoclonal antibody", thus any "antibody" of claim 1 is necessarily a "monoclonal antibody".

Claim 9 is vague and indefinite because it is dependent on a non-elected claim. Furthermore, it is improper because it referenced two set of claims with different features.

Claim 10, "a monoclonal antibody" should be changed to -The monoclonal antibody— for clarity.

Claims 11, 14 and 26-31 are vague and indefinite because they are methods with no method steps. It is unclear how the 19P2 ligand is "assayed" or detected. Claims 26-31, "A method" should be changed to -The method— for clarity.

Claim 15 is vague and indefinite because it is unclear how hyperprolactinemia is diagnosed using an assay method that detects 19P2 ligand. There is no information correlating the detection of 19P2 ligand with hyperprolactinemia. Furthermore, claim 15 is a method with no method steps. Claim 15 also lacks antecedent support in the specification as originally filed.

Claims 18-20, "a monoclonal antibody" should be changed to -The monoclonal— for clarity. These claims are also vague and indefinite because it is unclear how one monoclonal antibody can specifically bind to different peptides. It is requested that Applicant point to the specific amino acids to which the antibody specifically binds.

Claim 21, "A monoclonal antibody" should be changed to -The monoclonal antibody— for clarity.

Claims 27 and 28 are vague and indefinite with respect to the recitation of "a monoclonal antibody is attached" because it is unclear which monoclonal antibody is being claimed.

Claim Rejections - 35 USC § 112, first paragraph

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claim 25 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification fails to provide an adequate written description of the invention and fails to provide an enabling disclosure, because the specification does not provide evidence that the claimed biological materials are: (1) known and readily available to the public; (2) reproducible from the written description; or, (3) deposited in compliance with the criteria set forth in 37 CFR " 1.801-1.809."

The specification lacks complete deposit information for the hybridoma P2L-1T deposited as FERM-BP-6300. Because it is not clear that the cell line possessing the properties of the hybridoma designated P2L-1T is known and publicly available or can be reproducibly isolated without undue experimentation, and because the invention claims or uses the hybridoma and monoclonal antibodies produced by that hybridoma, a suitable deposit for patent purposes is

required. Accordingly, filing of evidence of the reproducible production of the cell lines and antibodies necessary to practice the instant invention or filing of evidence of deposit is required. Without a publicly available deposit of the above cell lines, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the cell lines is an unpredictable event. Applicants must comply with the criteria set forth in 37 CFR 1.801-1.809.

If the deposits are made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicant, or a statement by an attorney of record over his or her signature and registration number, stating that the specific cell lines have been deposited under the Budapest Treaty, that the cell lines will be irrevocably and without restriction or condition released to the public upon the issuance of a patent and that the cell lines will be replaced should they ever become non-viable, would satisfy the deposit requirement made herein.

If the deposits have not been made under the Budapest Treaty, then in order to certify that the deposits meet the criteria set forth in 37 CFR 1.801-1.809, applicant may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

- during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
- all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

- the deposits will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;
- the deposits were viable at the time of deposit; and,
- that the deposits will be replaced if they should ever become non-viable.

13. In the instant case, it is not clear that the deposit was made under the terms of the Budapest Treaty, nor is there available a viability statement, i.e. one certifying that the deposit was viable at the time of the deposit or a certificate verifying such from the depository. As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit along with the necessary statements in order to meet the criteria se forth in 37 CFR 1.801-1.809. Furthermore, the address of the depository is not disclosed in full in the specification.

Applicant's attention is directed to In re Lundak, 773 F.2nd. 1216, 227 USPQ 90 (CAFC 1985) and 37 CRF 1.801-1.809 for further information concerning deposit practice.

14. Claims 6, 21 and 31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention because the specification lacks deposit information for the monoclonal antibody designated P2L-1Ta.

15. Claims 4, 5, 7-11, 14, 15, 18-20 and 26-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for monoclonal antibodies designated P2L-1Ta, P2L-3Ta and a hybridoma cell line designated P2L-1T having deposit number FERM-BP-6300,

does not reasonably provide enablement for any other monoclonal antibody that can specifically bind to an intermediate partial peptide of the 19P2 ligand. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification at pages 20-24 teaches that monoclonal antibodies P2L-1Ta and P2L-3Ta specifically reacts with an intermediate partial peptide of the 19P2 ligand such as a partial peptide having the amino acid sequence SEQ ID NO. 11, and method for detecting 19P2 ligand using the same. The specification does not teach any other monoclonal antibodies reactive with an intermediate partial peptide of the 19P2 ligand.

16. Claim 15 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

Claim 15 recites a method for diagnosing hyperprolactinemia comprising the detection of 19P2 ligand. Such a method does not have support in the specification as filed. The specification at page 2, line 23 teaches that the 19P2 ligand is a hypothalamic hormone and is

considered to have some function involving pituitary hormones. However, its physiological functions are not completely known. Nowhere in the specification is there are teaching of how 19P2 relates to hyperprolactinemia and whether such a disease can be correlated with 19P2.

According to the prior art, specifically, Strongin (1993, "Sensitivity, Specificity, and Predictive Value of Diagnostic Tests: Definitions and Clinical Applications", in Laboratory Diagnosis of Viral Infections, Lennette, e., ed., Marcel Dekker, Inc., New York, pp. 211-219) a number of characteristics need to be considered in the development of any suitable diagnostic assay. These characteristics include the following: (1) the sensitivity of the assay; (2) the true-positive test rate; (3) the false-negative test rate; (4) the specificity, or percentage of patients without the disease who will display a negative results; (5) the true-negative test rate; (6) the false-positive test rate; (7) the predictive value, or the probability that the test result is correctly indicating the presence or absence of the disease; (8) the prevalence, or number of patients in any given population that have the disease in question; (9) the efficiency or percentage of all results that are true; (10) the accuracy of the recited diagnostic assay. Additional considerations must also be examined to enable the clinician to practice the invention including assessment of the following: (1) when is the maximum sensitivity desired?; (2) when is the maximum specificity desired?; (3) when is the maximum efficiency desired?; (4) How is the maximum sensitivity or specificity achieved?; (5) how is the predictive value maximized? An essential understanding of these factors is required to enable the skilled artisan to accurately use and interpret any given diagnostic test.

Since the specification lacks any teaching of how the diagnostic tests were performed, or any information regarding the patients from which the samples were taken, how the detected protein is related to the specific disease, and whether any considerations were given to any of

the characteristics state above, therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 4, 5, 7-11, 14, 18-20 and 26-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Hinuma et al (WO 97/24436).

Hinuma discloses G-protein coupled receptors and their ligands and method for making and using monoclonal antibodies to the same. See pages 77 and 78. Hinuma also teaches sandwich and competitive assays using the monoclonal antibody to detect a ligand polypeptide or a G-protein coupled receptor in a sample. See page 81.

Allowable Subject Matter

19. Claims 6, 21 and 31 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

20. Claims 6, 21 and 31 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

21. The following is a statement of reasons for the indication of allowable subject matter: the prior art of record fail to teach a monoclonal antibody designated as P2L-1Ta nor does it teach a hybridoma cell line designated as P2L-1Ta.

Conclusion

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy L. Nguyen whose telephone number is (571) 272-0824. The examiner can normally be reached on Tuesday and Thursday from 9:00 a.m. - 4:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao-Thuy L. Nguyen
Primary Examiner
Art Unit 1641

11 March 2004